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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
10/047,072	01/15/2002	Ralph M. Steinman	MER-01ICN 112917-144	7452

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/047,072	Sreinman et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *10/15/02 and 1/15/02* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-6 and 10-12* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6 and 10-12* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Compliance*

DETAILED ACTION

1. As filed, the instant application recited Claims 1, 2, 3, 4, 5, 6, 5, 7, and 8. Under Rule 1.126, the second Claim 5 was renumbered Claim 7, Claim 7 was renumbered Claim 8, and Claim 8 was renumbered Claim 9. Accordingly, Claims 9-11 in the amendment filed 1/15/03 have been renumbered 10-12, respectively.

Claims 7-9 have been canceled.
Claims 1-6 and 10-12 are being acted upon.

2. Applicant's election of the cytokine IL-4 in Claim 6, with traverse, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the species requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, the sequences at pages 31 and 61 of the specification must be identified by SEQ ID NO: and the specification must be brought into compliance with sequence rules.

4. A review of the claims raises the question of whether of not Applicant intended that this application be filed as a Continuation or possibly a Continuation-in-Part (comprising some additional disclosure) because the claims do not seem to fit the specification. The specification discloses a method for producing mature stable dendritic cells (DCs) from immature DCs employing a "maturation factor". The instant claims however, simply refers to generic DCs and a "factor" which allows them to "mature and express characteristics of DCs". Note that the claims recite "pluripotential cells", including "mononuclear pluripotential cells" (Claim 2) and "pluripotential cells" that are monocytes (Claim 4), however, the only "pluripotential cells" disclosed in the specification are PBMCs. Further, the specification makes clear that culture in GM-CSF alone (Claim 5) will result in a cell that reverts to a macrophage-like phenotype upon removal of the cytokine. Finally note, most of the cytokines recited in Claim 6 are not disclosed in the instant specification or claims of the '483 parent application.

Applicant is invited to clarify this issue, however, for art purposes, the claims will be considered to comprise a method of culturing any DC precursor, or monocyte (Claim 4) with GM-CSF, or GM-CSF and IL-4 (Claims 6 and 7).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-6 and 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) The term "pluripotential cells" is vague and indefinite as the term is not defined in the specification and just one example of "pluripotential cells" (PBMCs) are disclosed. It is unclear whether the terms are meant to be interchangeable or whether other types of "pluripotential cells" are encompassed by the claims.

B) The phrase "express characteristics of DCs" is vague and indefinite as said "characteristics" are not defined in the specification. It is noted that some "properties of mature DCs" are disclosed at pages 55-56 of the specification but it is unclear whether or not these comprise the "characteristics" of the claims.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

8. Claims 1-6 and 10-12 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent No. 5,994,126.

The '126 patent teaches an *in vitro* method of producing DCs comprising culturing pluripotential cells comprising monocytes (which are inherently $CD14^+$) or mononuclear cells (both components of PBMCs) in about 200U/ml to about 2000U/ml of a "factor" comprising GM-CSF and additionally IL-4 (see particularly column 16, lines 43-45 and Example 1). Note that Claims 11 and 12 merely recite well known properties inherent to DCs, i.e., high level expression of MHC molecules and the capacity to stimulate resting T cells.

The reference clearly anticipates the claimed invention.

9. Claims 1-6 and 10-12 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Romani et al. (1994).

Romani et al. teaches an *in vitro* method of producing DCs comprising culturing pluripotential cells comprising monocytes (which are inherently $CD14^+$) or mononuclear cells (both components of PBMCs) in about 200U/ml to about 2000U/ml of a "factor" comprising GM-CSF and additionally IL-4 (see particularly page 84, **Materials and Methods**). Note that Claims 11 and 12 merely recite well known properties inherent to DCs, i.e., high level expression of MHC molecules and the capacity to stimulate resting T cells.

The reference clearly anticipates the claimed invention.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-6 and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that Applicant was in possession of a <u>factor</u> in which to culture pluripotential cells which would cause them to express

characteristics of DCs. The specification discloses that "The mature dendritic cells are prepared according to this invention by contacting the immature dendritic cells with a dendritic cell maturation factor. As referred to herein, the dendritic cell maturation factor may actually be one or more specific substances which act in concert to cause the maturation of the immature dendritic cells. Such a factor has been determined to be present in PBMC conditioned medium, preferrably [*sic*] monocyte conditioned medium." Thus, while the specification discloses a "dendritic cell maturation factor", this passage makes clear that Applicant had no idea what "dendritic cell maturation factor" actually consisted of, but rather Applicant knew only a method/source for obtaining said "factor". Regarding the more generic "factor" of the instant claims, the specification is silent. One of skill in the art must therefore conclude then that the specification fails to disclose a representative number of species to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 at (703) 305-3014. The CM1 Fax Center telephone numbers are 703-872-9306 (before final) and 703-872-9307 (after final).

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600
March 31, 2003